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GUIDANT

CONTAK RENEWAL® 3
CONTAK RENEWAL® 3 HE

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RESTRICTED DEVICE:
Federal law (USA) restricts this device to sale, distribution, and use by, or on the lawful order of a physician trained or experienced in device implant and follow-up procedures.

System Guide

CONTAK RENEWAL® 3
MODELS H170/H175

CONTAK RENEWAL® 3 HE
MODELS H177/H179

Cardiac Resynchronization Therapy Defibrillator

GUIDANT

ABOUT THIS MANUAL

This System Guide contains information about the CONTAK RENEWAL 3 cardiac resynchronization therapy defibrillator (CRT-D) used with the Model 2845 CONSULT Software Application and the ZOOM® Programming System, which includes the Model 2920 Programmer/Recorder/Monitor (PRM).

The CONTAK RENEWAL 3 family of products includes the CONTAK RENEWAL 3 and the CONTAK RENEWAL 3 HE devices. This manual is written for full description of both devices. All PRM screen illustrations in this manual show typical screens for both devices. The screens you see when interrogating or programming the pulse generator will be similar, depending on the programmed parameters.

Throughout this manual, the following text conventions will be used:

PRM KEYS	The names of the PRM keys will appear in capital letters (eg, PROGRAM, INTERROGATE).
Screen Text	When text appearing on the PRM screen is referred to in the manual, it will appear with the first letter of each word capitalized.
1., 2., 3.	Numbered lists indicate a series of instructions that should be followed in the order given.
•	Bullets precede items in a list, or a series that is not sequential.

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RATE ENHANCEMENTS SUBMENU

LEAD CONFIGURATION SUBMENU

AV DELAY SUBMENU

INFORMATION FOR USE

CHAPTER 1

This chapter contains the following topics:

DEVICE DESCRIPTION

The Guidant CONTAK RENEWAL® 3 cardiac resynchronization therapy defibrillator (CRT-D), Models H170 and H175, and CONTAK RENEWAL® 3 HE CRT-D, Models H177 and H179, provide ventricular tachyarrhythmia and cardiac resynchronization therapies. Ventricular tachyarrhythmia therapy is for the treatment of ventricular tachycardia (VT) and ventricular fibrillation (VF), rhythms that are associated with sudden cardiac death (SCD). Cardiac resynchronization therapy is for the treatment of heart failure (HF) and uses biventricular electrical stimulation to synchronize ventricular contractions. The device also uses accelerometer-based adaptive-rate bradycardia therapy similar to Guidant's commercially available VENTAK® family of implantable cardioverter defibrillators (ICDs). The pulse generator has independently programmable outputs and accepts one IS-1[1] atrial lead, one LV-1 or one IS-1 coronary venous pace/sense lead, and one DF-1/IS-1 cardioversion/ defibrillation lead. The pulse generator and the leads constitute the implantable portion of the CONTAK RENEWAL 3 system. The device's small, physiologic shape minimizes pocket size and may minimize device migration.

Cardioversion/defibrillation therapies include a range of low- and high-energy shocks using either a biphasic or monophasic waveform. The CONTAK RENEWAL 3 device uses the Guidant TRIAD electrode system for defibrillation energy delivery. By using the metallic housing of the pulse generator as an active electrode, combined with the Guidant ENDOTAK® two-electrode defibrillation lead, energy is sent via a dual-current pathway from the distal shocking electrode to the proximal electrode and to the pulse generator case. The CONTAK RENEWAL 3 device also offers a wide variety of antitachycardia pacing schemes to terminate slower, more stable ventricular tachyarrhythmias. Bradycardia pacing with cardiac resynchronization therapy, including adaptive-rate features, is available to detect and treat bradyarrhythmias and to support the cardiac rhythm after defibrillation therapy.

The ZOOM® Programming System, which includes the Model 2920 Programmer/ Recorder/Monitor (PRM), the Model 2845 CONSULT Software Application, and an accessory telemetry wand, constitutes the external portion of the CONTAK RENEWAL 3 system. The external components allow interrogation and programming of the pulse generator as well as access to the device's diagnostic features. The CONTAK RENEWAL 3 system can be programmed to provide a variety of therapy options. It also can provide noninvasive diagnostic testing and therapy history data.

1. IS-1 refers to the international standard ISO 5841.3:2000. LV-1 refers to the Guidant LV® proprietary connector. DF-1 refers to the international standard ISO 11318:2002.

Related Manuals and Information Tools

The Operator's Manual for the Guidant Programmer/Recorder/Monitor provides information specific to the programmer, such as setting up the system, maintenance, and handling. Physician's manuals for the leads provide specific information and instructions regarding the implanted leads. The Physician's Technical Manual is packaged with the pulse generator and provides the information needed to implant the device at nominal parameter settings. All information in the Physician's Technical Manual is also included in this manual.

INDICATIONS AND USAGE

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (EF ≤ 35%) and QRS duration ≥ 120 ms.

CLINICAL OUTCOMES

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) have demonstrated the following outcomes in the indicated population specified above:

- Reduction in risk of all-cause mortality or first hospitalization, where a hospitalization is defined as either:
  - — Care provided at a hospital for any reason in which the duration is associated with a date change, or
  - — Use of intravenous inotropes and/or vasoactive drugs for a duration > 4 hours (inpatient or outpatient).

NOTE: *Hospitalizations associated with a device implant attempt or re-attempt are excluded.*

- Reduction in risk of all-cause mortality
- Reduction of heart failure symptoms

CONTRAINDICATIONS

There are no contraindications for this device.

WARNINGS

General

- **Labeling knowledge.** Read this manual thoroughly before implanting the pulse generator to avoid damage to the system. Such damage can result in injury to or death of the patient.

- **Avoid shock during handling.** Program the pulse generator Tachy Mode to Off during implant, explant, or postmortem procedures to avoid inadvertent high voltage shocks.

- **Defibrillator paddles.** Always have sterile external and internal defibrillator paddles or an equivalent (e.g., R2[2] pads) immediately available during conversion testing. If not terminated in a timely fashion, an induced tachyarrhythmia can result in the patient's death.

- **Resuscitation availability.** Ensure that an external defibrillator and medical personnel skilled in cardiopulmonary resuscitation (CPR) are present during post-implant device testing should the patient require external rescue.

- **Magnetic resonance imaging (MRI) exposure.** Do not expose a patient to MRI device scanning. Strong magnetic fields may damage the device and cause injury to the patient.

- **Diathermy.** Do not subject a patient with an activated implanted pulse generator to diathermy since diathermy may damage the pulse generator.

Programming and Device Operation

- **Atrial tracking modes.** Do not use atrial tracking modes in patients with chronic refractory atrial tachyarrhythmias. Tracking of atrial arrhythmias could result in VT or VF.

- **Atrial only modes.** Do not use atrial only modes in patients with heart failure because such modes do not provide cardiac resynchronization therapy.

- **Ventricular sensing.** Left ventricular lead dislodgment to a position near the atria can result in atrial oversensing and left ventricular pacing inhibition. See Sensitivity Adjustment on page 10-4 for more information.

2. Trademark of the R2 Corporation.

- **Slow VT.** Physicians should use medical discretion when implanting this device in patients who present with slow VT. Programming therapy for slow monomorphic VT may preclude CRT delivery at faster rates if these rates are in the tachyarrhythmia zones. See CRT Delivery Zone and Tachyarrhythmia Zones on page 3-5 for more information.

Implant Related

- **Do not kink leads.** Kinking leads may cause additional stress on the leads, possibly resulting in lead fracture.

- **Patch leads.** Do not use defibrillation patch leads with the CONTAK RENEWAL 3 system, or injury to the patient may occur.

- **Separate pacemaker.** Do not use the CRT-D device with a separate pacemaker system. This combination could result in CRT-D/pacemaker interaction.

- **Emulator.** The emulator is not intended for use as a permanent lead electrode and must be removed from the patient. It is for one-time use only. Do not resterilize.

PRECAUTIONS

Sterilization, Storage, and Handling

- **For single use only—do not resterilize devices.** Do not resterilize the device or the accessories packaged with it because Guidant cannot ensure that resterilization is effective.

- **If package is damaged.** Guidant sterilizes the pulse generator blister trays and contents with ethylene oxide gas before final packaging. When the pulse generator is received, it is sterile, provided the container is intact. If the packaging is wet, punctured, opened, or otherwise damaged, return the device to Guidant.

- **Storage temperature and equilibration.** Recommended storage temperatures are 0°C–50°C (32°F–122°F). Allow the device to reach room temperature before programming or implanting the device because temperature extremes may affect initial device function.

- **Device storage.** Store the pulse generator in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI) to avoid device damage.

- **Use before date.** Implant the device system before the USE BEFORE date on the package label because this date reflects a validated shelf life. For example, if the date is January 1, do not implant on or after January 1.

Implantation and Device Programming

- **Lead system.** Do not use any lead with this device without first verifying connector compatibility. Using incompatible leads can damage the connector or result in potential adverse consequences, such as undersensing of cardiac activity or failure to deliver necessary therapy.

- **STAT PACE settings.** Do not leave the device programmed in STAT PACE settings; these settings may significantly reduce the lifetime of the device due to the high output.

- **Drug-resistant SVTs.** Determine if the device and programmable options are appropriate for patients with drug-resistant supraventricular tachyarrhythmias (SVTs), because drug-resistant SVTs can initiate unwanted tachyarrhythmia therapy or can cause inhibition of cardiac resynchronization therapy.

- **AV Delay.** For delivery of cardiac resynchronization therapy, the programmed setting for the AV Delay must be less than the patient's intrinsic intracardiac AV interval.

- **Adaptive-rate pacing.** The clinical benefit of adaptive-rate pacing in heart failure patients has not been studied. The use of adaptive-rate pacing should be used with medical discretion only if the patient develops an indication for rate-responsive pacing, such as chronotropic incompetence. Patients with heart failure may have hemodynamic compromise at rapid sensor-driven rates, and the physician may wish to program less aggressive adaptive-rate parameters in accordance with patient condition.

- **Atrial Tachy Response (ATR).** ATR should be programmed Off unless the patient has a history of atrial tachyarrhythmias. The delivery of CRT is compromised because AV synchrony is disrupted.

- **Threshold test.** During the left ventricular threshold test, right ventricular backup pacing is unavailable.

- **Left ventricular pacing only.** The clinical effect of left ventricular pacing alone for heart failure patients has not been studied.

- **Do not bend the lead near the lead–header interface.** Improper insertion can cause insulation damage near the terminal ring that could result in lead failure.

- **Shock waveform polarity.** Never change the shock waveform polarity by physically switching the lead anodes and cathodes in the pulse generator header—use the programmable Polarity feature. Device damage or nonconversion of the arrhythmia post-operatively may result if polarity is switched physically.

- **Absence of an LV lead.** Absence of an electrode or plug in the LV lead port may affect device performance. If an LV lead is not used, be sure to insert a plug.

- **Electrode connections.** Fully insert each IS-1 or LV-1 pace/sense lead into its lead port and then tighten the setscrews onto the electrodes. If the lead is not fully inserted, the setscrews might damage the lead body.

- **Tachy Mode to Off.** Ensure that the pulse generator's Tachy Mode is Off when not in use, before handling it, and before using electrosurgery to prevent inappropriate shocks. For tachyarrhythmia therapy, verify that the Tachy Mode is on.

- **Atrial oversensing.** Care must be taken to ensure that artifacts from the ventricles are not present on the atrial channel or atrial oversensing may result. If ventricular artifacts are present in the atrial channel, the atrial lead may need to be repositioned to minimize its interaction.

- **Defibrillation lead impedance.** Never implant the device with a lead system that has less than 15-Ω total shock lead impedance. Device damage may result. If a shocking lead impedance is less than 20 Ω, reposition the shocking electrodes to allow a greater distance between the shocking electrodes.

- **ATR Entry Count.** Exercise care when programming the Entry Count to low values in conjunction with a short duration. This combination allows mode switching with very few fast atrial beats. If the entry count were programmed to 2 and the duration to 0, for example, ATR mode switching could occur on two fast atrial intervals. In these instances, a short series of premature atrial events could cause the device to mode switch.

- **ATR Exit Count.** Exercise care when programming the Exit Count to low values. If the Exit Count were programmed to 2, for example, a few cycles of atrial undersensing could cause termination of mode switching.

- **Left ventricular lead configuration.** Proper programming of the LV coronary venous lead configuration is essential for proper LV lead function. Program the lead configuration in accordance with the number of electrodes on the LV lead; otherwise, erratic LV sensing, loss of LV pacing, or ineffective LV pacing might occur.

- **Left Ventricular Protection Period (LVPP).** Use of a long LVPP reduces the maximum left ventricular pacing rate and may inhibit cardiac resynchronization therapy at higher pacing rates.

- **Shunting energy.** Do not allow any object that is electrically conductive to come into contact with the lead or device during induction because it may shunt energy and result in less energy getting to the patient, and may damage the implanted system.

- **Sensing adjustment.** Following any sensing range adjustment or any modification of the sensing lead, always verify appropriate sensing for HF/ bradycardia pacing and tachycardia detection.

Follow-up Testing

- **Conversion testing.** Successful conversion of ventricular fibrillation or ventricular tachycardia during arrhythmia conversion testing is no assurance that conversion will occur post-operatively. Be aware that changes in the patient's condition, drug regimen, and other factors may change the defibrillation threshold (DFT), which may result in nonconversion of the arrhythmia post-operatively.

Pulse Generator Explant and Disposal

- **Incineration.** Be sure that the pulse generator is removed before cremation. Cremation and incineration temperatures might cause the pulse generator to explode.

- **Device handling.** Program the pulse generator Tachy Mode to Off, disable the magnet feature, and disable the Beep When ERI Is Reached beeper before

explanting, cleaning, or shipping the device to prevent unwanted shocks, overwriting of important therapy history data, and audible tones.

- **Explanted devices.** Return all explanted pulse generators and leads to Guidant.

Environmental and Medical Therapy Hazards

- **Avoiding electromagnetic interference (EMI).** Advise patients to avoid sources of EMI because EMI may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy. Examples of EMI sources are: electrical power sources, arc welding equipment and robotic jacks, electrical smelting furnaces, large RF transmitters such as RADAR, radio transmitters including those used to control toys, electronic surveillance (anti-theft) devices, and an alternator on a car that is running.

Hospital and Medical Environments

- **Do not use internal defibrillation** paddles unless the pulse generator is disconnected from the leads because it may shunt energy causing injury to the patient, and may damage the pulse generator.

- **External defibrillation.** Use of external defibrillation can damage the pulse generator. To help prevent defibrillation damage to the pulse generator: position the defibrillation paddles as far from the pulse generator as possible, position the defibrillation paddles perpendicular to the implanted pulse generator–lead system, and set energy output of defibrillation equipment as low as clinically acceptable.

  Following any external defibrillation episode, verify pulse generator function since external defibrillation may have damaged the pulse generator. To verify proper function: interrogate the device, perform a manual capacitor re-formation, verify battery status, check the shock counters, and ensure that programmable parameters did not change.

- **Electrical interference** or "noise" from devices such as electrosurgical and monitoring equipment may interfere with establishing or maintaining telemetry for interrogating or programming the device. In the presence of such interference, move the programmer away from electrical devices and ensure that the wand cord and cables are not crossing one another.

- **Electrosurgical cautery.** Do not use electrosurgery devices until the pulse generator's tachyarrhythmia therapy is deactivated. If active, the pulse generator may deliver an inappropriate shock to the patient. Remember to reactivate the pulse generator after turning off the electrosurgery equipment.

- **Ionizing radiation therapy may adversely affect device operation.** During ionizing radiation therapy (e.g., radioactive cobalt, linear accelerators, and betatrons), the pulse generator must be shielded with a radiation-resistive material, regardless of the distance of the device to the radiation beam. Do not project the radiation port directly at the device. After waiting a minimum of one hour following radiation treatment (to allow for a device memory check to occur), always evaluate device operation including interrogation and sensing and pacing threshold testing. At the completion of the entire course of treatments, perform device interrogation and follow-up, including sensing and pacing threshold testing and capacitor re-formation.

- **Lithotripsy may damage the pulse generator.** If lithotripsy must be used, avoid focusing near the pulse generator site.

- **Therapeutic ultrasound energy may damage the pulse generator.** If therapeutic ultrasound energy must be used, avoid focusing near the pulse generator site.

- **Radio frequency ablation.** Exercise caution when performing radio frequency ablation procedures in device patients. If the pulse generator Tachy Mode is programmed On during the procedure, the device may inappropriately declare a tachycardia episode and deliver therapy, or may cause inhibition of pacing therapy. Minimize risks by following these steps:

  — Program the Tachy Mode to Off to avoid inadvertent tachycardia detection (sensing) or therapy.

  — Avoid direct contact between the ablation catheter and the implanted lead and pulse generator.

  — Keep the current path (electrode tip to ground) as far away from the pulse generator and leads as possible.

  — Have external defibrillation equipment available.

  — Consider the use of external pacing support for pacemaker-dependent patients.

Home and Occupational Environments

- **Static magnetic fields.** Advise patients to avoid equipment or situations where they would have extended exposure to strong (>10 gauss or 1 mTesla) magnetic fields since the pulse generator mode could change. To prevent mode change in the presence of magnets, the Change Tachy Mode With Magnet feature may be programmed Off. Examples of magnetic sources are: industrial transformers and motors, magnetic resonance imaging (MRI) devices, large stereo speakers, telephone receivers if held within 0.5 inches (1.27 cm) of the pulse generator, and magnetic wands such as those used for airport security and in the game "Bingo."

Electronic Article Surveillance (EAS)

- Advise patients to avoid lingering near anti-theft devices, such as those found in entrances and exits of department stores and public libraries, and to walk through them at a normal pace, because such devices may cause inappropriate pulse generator operation.

Cellular Phones

- Advise patients to hold cellular phones to the ear opposite the side of the implanted device. Patients should not carry a cellular phone in a breast pocket or on a belt over or within 6 inches (15 cm) of the implanted devices since some cellular phones may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy.

OBSERVED ADVERSE EVENTS

Prior History

The CONTAK RENEWAL 3, CONTAK RENEWAL, and CONTAK CD devices provide the same defibrillation and cardiac resynchronization therapy (biventricular pacing) and have the same Indications for Use. Therefore, the Comparison of Medical, Pacing, and Defibrillation Therapies in Heart Failure (COMPANION) clinical trial data (based on CONTAK CD devices) used to support expanding Guidant CRT-D indications to the COMPANION patient population, are also applicable to CONTAK RENEWAL and CONTAK RENEWAL 3.

The primary difference between CONTAK CD devices and CONTAK RENEWAL/ CONTAK RENEWAL 3 devices is that CONTAK CD utilizes an electrically common

RV and LV sensing/pacing circuit whereas CONTAK RENEWAL and CONTAK RENEWAL 3 incorporate an independent RV and LV sensing/pacing circuit. Additional clinical analysis was conducted with CONTAK RENEWAL, in a European study, to provide confirmation that the independent sensing and pacing capability did not adversely affect the ability of the device to detect ventricular tachyarrhythmias or provide continuous biventricular pacing therapy.

COMPANION Study Background

The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Study was a prospective, open-label, randomized, controlled, multi-center, unblinded study conducted at 128 sites and enrolled a total of 1638 patients, of which 1520 were randomized. Patients were randomly assigned 1:2:2 to receive optimal pharmacological therapy (OPT, 308 patients) or a cardiac resynchronization therapy pacemaker (CRT-P, 617 patients) or a cardiac resynchronization therapy pacemaker with defibrillator (CRT-D, 595 patients). Of the 1520 patients randomized, 903 were randomized to OPT and CRT-D. This summary focuses on data and analyses for the CRT-D and OPT groups, only, with the exception of the Exercise Performance results, which are based on pooled CRT-D and CRT-P data.

The CRT-D devices (CONTAK CD) in this trial, were approved for commercial distribution via the CONTAK CD study, which provided a reasonable assurance of safety. A similar safety analysis was applied to the COMPANION patient population. The results were consistent with safety measurements obtained in the CONTAK CD trial. See "Data Analysis and Results: CRT-D System Safety" on page 1-45.

Adverse Event Definitions

Adverse events were defined as any undesirable clinical occurrence, whether it was related to the device or not. Table 1-1 includes adverse events occurring in the first six months related to the device (pulse generator and leads) and implant procedures (including attempts). Table 1-2 includes adverse events occurring in the first six months related to patient condition (i.e., worsening heart failure). Adverse events are listed in descending order by total number of patients experiencing the event.

Adverse events related to the device were further reported using two sub-categories based on the nature of the intervention. These events were defined as a *complication* if the event resulted in invasive intervention, loss of significant device function, and death or permanent disability. An *observation* was a device-related

adverse event that was resolved non-invasively. Forty-nine percent of CRT-D patients reported a device and/or procedure-related adverse event.

Table 1-1. Device- and Procedure-Related Adverse Events Occurring During the First Six Months Post Randomization[a] (N = 588)

	Total Events (Patients)	% Comps (Patients)	% Obs (Patients)
Total Adverse Events	**498 (290)**	**13.1 (77)**	**43.4 (255)**
Post surgical wound discomfort	68 (62)	0.0 (0)	10.5 (62)
Phrenic nerve/diaphragm stimulation	77 (59)	1.4 (8)	9.0 (53)
Brady capture - LV	38 (36)	4.3 (25)	2.2 (13)
Hematoma	37 (34)	0.3 (2)	5.4 (32)
Inappropriate shock above rate cutoff	26 (24)	0.0 (0)	4.1 (24)
Multiple counting - tachy	22 (17)	0.3 (2)	2.9 (17)
Pocket infection	19 (17)	0.5 (3)	2.6 (15)
Dissection, coronary sinus	15 (15)	0.0 (0)	2.6 (15)
Brady capture - atrium	14 (12)	1.5 (9)	0.5 (3)
Inappropriate shock due to oversensing	11 (11)	0.0 (0)	1.9 (11)
Pneumothorax	10 (10)	1.0 (6)	0.7 (4)
Hypotension	10 (9)	0.2 (1)	1.4 (8)
Brady capture - RV	8 (8)	0.9 (5)	0.5 (3)
Physical trauma	8 (8)	0.2 (1)	1.2 (7)
AV Block - heart block, complete	7 (7)	0.2 (1)	1.0 (6)
Pacemaker-mediated tachycardia (PMT)	7 (6)	0.0 (0)	1.0 (6)
Physiological reaction[b]	6 (6)	0.0 (0)	1.0 (6)
Arrhythmia - atrial fibrillation	5 (5)	0.0 (0)	0.9 (5)
Bleeding/fluid accumulation	5 (5)	0.0 (0)	0.9 (5)
Perforation, coronary venous	5 (5)	0.5 (3)	0.3 (2)
Renal failure	5 (5)	0.0 (0)	0.9 (5)
Thrombosis	5 (5)	0.0 (0)	0.9 (5)
Vascular related	5 (5)	0.0 (0)	0.9 (5)
Oversensing - atrium pace sense	4 (4)	0.3 (2)	0.3 (2)
Allergic reaction	3 (3)	0.0 (0)	0.5 (3)
Congestive heart failure	3 (3)	0.0 (0)	0.5 (3)
Nausea (2), Constipation (1)	3 (3)	0.0 (0)	0.5 (3)

Table 1-1. Device- and Procedure-Related Adverse Events Occurring During the First Six Months Post Randomization[a] (N = 588)

	Total Events (Patients)	% Comps (Patients)	% Obs (Patients)
High DFTs - tachy	3 (3)	0.2 (1)	0.3 (2)
Oversensing - ventricle rate - tachy	3 (3)	0.2 (1)	0.3 (2)
Respiratory related	3 (3)	0.2 (1)	0.3 (2)
Ventricular tachycardia	3 (3)	0.2 (1)	0.3 (2)
Cardiac tamponade	2 (2)	0.3 (2)	0.0 (0)
Dyspnea (shortness of breath)	2 (2)	0.0 (0)	0.3 (2)
Electrolyte/lab	2 (2)	0.0 (0)	0.3 (2)
Hemorrhage	2 (2)	0.2 (1)	0.2 (1)
Insulation breach suspected	2 (2)	0.3 (2)	0.0 (0)
Migration of device	2 (2)	0.0 (0)	0.3 (2)
Muscle stimulation	2 (2)	0.0 (0)	0.3 (2)
Myocardial infarction	2 (2)	0.0 (0)	0.3 (2)
Numbness	2 (2)	0.0 (0)	0.3 (2)
Perforation, venous	2 (2)	0.0 (0)	0.3 (2)
Phantom shock	2 (2)	0.0 (0)	0.3 (2)
Undersensing - atrium pace sense - brady	2 (2)	0.2 (1)	0.2 (1)
Altered hemodynamic status	1 (1)	0.0 (0)	0.2 (1)
Arrhythmia	1 (1)	0.0 (0)	0.2 (1)
Arrhythmia - sinus tachycardia	1 (1)	0.0 (0)	0.2 (1)
Bruise	1 (1)	0.0 (0)	0.2 (1)
Cardiac arrest	1 (1)	0.2 (1)	0.0 (0)
Change in arrhythmia - SVT	1 (1)	0.0 (0)	0.2 (1)
Change in arrhythmia - brady	1 (1)	0.0 (0)	0.2 (1)
Change in arrhythmia - junctional	1 (1)	0.0 (0)	0.2 (1)
Change in physical status	1 (1)	0.0 (0)	0.2 (1)
Chest pain	1 (1)	0.0 (0)	0.2 (1)
Dizziness, cause undetermined	1 (1)	0.0 (0)	0.2 (1)
Edema	1 (1)	0.0 (0)	0.2 (1)
Fatigue	1 (1)	0.0 (0)	0.2 (1)
Febrile	1 (1)	0.0 (0)	0.2 (1)
Unable to urinate	1 (1)	0.0 (0)	0.2 (1)

Table 1-1. Device- and Procedure-Related Adverse Events Occurring During the First Six Months Post Randomization[a] (N = 588)

	Total Events (Patients)	% Comps (Patients)	% Obs (Patients)
Helix related (screw tip), broken or stretched	1 (1)	0.2 (1)	0.0 (0)
Hemoglobin drop	1 (1)	0.2 (1)	0.0 (0)
Hypertension	1 (1)	0.0 (0)	0.2 (1)
Infection	1 (1)	0.2 (1)	0.0 (0)
Insulation breech observed	2 (1)	0.2 (1)	0.0 (0)
Malfunction, memory problem	1 (1)	0.2 (1)	0.0 (0)
Materials unretrieved in body	1 (1)	0.2 (1)	0.0 (0)
Pacemaker mediated tachycardia (PMT)	1 (1)	0.0 (0)	0.2 (1)
Pacemaker syndrome	1 (1)	0.0 (0)	0.2 (1)
Pericardial effusion	1 (1)	0.2 (1)	0.0 (0)
Pericarditis	2 (1)	0.0 (0)	0.2 (1)
Placement difficulty, stylet related	1 (1)	0.2 (1)	0.0 (0)
Pleural effusion	1 (1)	0.2 (1)	0.0 (0)
Pleurisy	2 (1)	0.0 (0)	0.2 (1)
Pocket erosion/extrusion	1 (1)	0.2 (1)	0.0 (0)
Anxiety	1 (1)	0.0 (0)	0.2 (1)
Respiratory arrest	1 (1)	0.2 (1)	0.0 (0)
Ventricular fibrillation	1 (1)	0.0 (0)	0.2 (1)

a. Observations and complications may not sum to total because some patient may have events in both categories.
b. Physiological reaction includes: swelling, rash, and/or drainage.

Table 1-2. Patient-Related Six Month Adverse Events

	Total Events (Patients)		% of Patients with Events		Events/Patient Year	
	CRT-D	OPT	CRT-D N = 595 Patients	OPT N = 308 Patients	CRT-D 281 Years	OPT 134 Years
Total Patient Related Adverse Events	**1437 (443)**	**625 (207)**	**74.5**	**67.2**	**5.11 (1437)**	**4.66 (625)**
Cardiovascular Related Events	**814 (351)**	**399 (176)**	**59.0**	**57.1**	**2.90 (814)**	**2.98 (399)**
Congestive heart failure[a]	269 (166)	185 (111)	27.9	36.0	0.96 (269)	1.38 (185)
Chest pain	83 (65)	50 (37)	10.9	12.0	0.30 (83)	0.37 (50)
Supraventricular tachyarrhythmia	69 (56)	11 (11)	9.4	3.6	0.25 (69)	0.08 (11)
Ventricular tachyarrhythmia	66 (51)	16 (15)	8.6	4.9	0.23 (66)	0.12 (16)
Electrolyte/lab	51 (42)	17 (16)	7.1	5.2	0.18 (51)	0.13 (17)
Hypotension	42 (40)	16 (15)	6.7	4.9	0.15 (42)	0.12 (16)
Dizziness, cause undetermined	33 (30)	26 (23)	5.0	7.5	0.12 (33)	0.19 (26)
Renal failure	40 (29)	16 (14)	4.9	4.5	0.14 (40)	0.12 (16)
Fatigue	27 (25)	12 (12)	4.2	3.9	0.10 (27)	0.09 (12)
Bradyarrhythmia	32 (30)	5 (5)	5.0	1.6	0.11 (32)	0.04 (5)
Vascular	14 (11)	11 (10)	1.8	3.2	0.05 (14)	0.08 (11)
Syncope	12 (12)	7 (7)	2.0	2.3	0.04 (12)	0.05 (7)
GI bleed	14 (13)	4 (4)	2.2	1.3	0.05 (14)	0.03 (4)
Arrhythmia	12 (10)	6 (6)	1.7	1.9	0.04 (12)	0.04 (6)
Hypertension	12 (9)	6 (5)	1.5	1.6	0.04 (12)	0.04 (6)
Palpitations	9 (9)	3 (3)	1.5	1.0	0.03 (9)	0.02 (3)
Myocardial infarction	7 (7)	4 (4)	1.2	1.3	0.02 (7)	0.03 (4)
Stroke syndrome or CVA	7 (7)	2 (2)	1.2	0.6	0.02 (7)	0.01 (2)
Deep vein thrombosis	4 (4)	0 (0)	0.7	0.0	0.01 (4)	0.00 (0)

Table 1-2. Patient-Related Six Month Adverse Events

	Total Events (Patients)		% of Patients with Events		Events/Patient Year	
	CRT-D	OPT	CRT-D N = 595 Patients	OPT N = 308 Patients	CRT-D 281 Years	OPT 134 Years
Transient ischemic attack (TIA)	3 (3)	1 (1)	0.5	0.3	0.01 (3)	0.01 (1)
Hematuria	3 (3)	0 (0)	0.5	0.0	0.01 (3)	0.00 (0)
Ischemia	2 (2)	1 (1)	0.3	0.3	0.01 (2)	0.01 (1)
Coagulopathy	2 (2)	0 (0)	0.3	0.0	0.01 (2)	0.00 0(0)
Bleeding/fluid accumulation	1 (1)	0 (0)	0.2	0.0	0.00 (1)	0.00 (0)
Non-cardiovascular Related Events	**623 (293)**	**226 (119)**	**49.2**	**38.6**	**2.22 (623)**	**1.69 (226)**
Respiratory related[b]	130 (108)	53 (41)	18.2	13.3	0.46 (130)	0.40 (53)
GI[c]	124 (95)	30 (24)	16.0	7.8	0.44 (124)	0.22 (30)
Pain	82 (66)	40 (32)	11.1	10.4	0.29 (82)	0.30 (40)
Physiological reaction[d]	76 (61)	20 (18)	10.3	5.8	0.27 (76)	0.15 (20)
Infection	54 (37)	18 (15)	6.2	4.9	0.19 (54)	0.13 (18)
Endocrine	41 (35)	16 (14)	5.9	4.5	0.15 (41)	0.12 (16)
Psychological effects	24 (19)	13 (12)	3.2	3.9	0.09 (24)	0.10 (13)
Change in physical status	20 (18)	9 (9)	3.0	2.9	0.07 (20)	0.07 (9)
Physical trauma	26 (22)	4 (4)	3.7	1.3	0.09 (26)	0.03 (4)
Neurologic	14 (14)	6 (6)	2.4	1.9	0.05 (14)	0.04 (6)
Genitourinary	9 (7)	5 (4)	1.2	1.3	0.03 (9)	0.04 (5)
Cancer, other	5 (5)	6 (5)	0.8	1.6	0.02 (5)	0.04 (6)
Febrile	7 (7)	0 (0)	1.2	0.0	0.02 (7)	0.00 (0)
Respiratory failure	4 (4)	1 (1)	0.7	0.3	0.01 (4)	0.01 (1)
Tumors, growths	1 (1)	2 (2)	0.2	0.6	0.00 (1)	0.01 (2)
Ulceration	2 (1)	2 (2)	0.2	0.6	0.01 (2)	0.01 (2)
Diabetes complications	2 (2)	0 (0)	0.3	0.0	0.01 (2)	0.00 (0)

Table 1-2. Patient-Related Six Month Adverse Events

	Total Events (Patients)		% of Patients with Events		Events/Patient Year	
	CRT-D	OPT	CRT-D N = 595 Patients	OPT N = 308 Patients	CRT-D 281 Years	OPT 134 Years
Pulmonary embolism	1 (1)	1 (1)	0.2	0.3	0.00 (1)	0.01 (1)
Pneumonia (respiratory infection)	1 (1)	0 (0)	0.2	0.0	0.00 (1)	0.00 (0)

a. Congestive heart failure includes: congestive heart failure, syspnea, volume overload, edema, pulmonary edema, change in drug therapy.
b. The most frequent three events in this category were: upper respiratory infection, bronchitis, and influenza.
c. The most frequent three events in this category were: nausea, diarrhea, and abdominal pain.
d. The most frequent three events in this category were: swelling, rash, and weight gain.

Deaths

There were a total of 182 deaths (77 OPT, 105 CRT-D) that occurred during the trial and recorded through November 30, 2002. Table 1-3 presents cause of death stratified by treatment group.

Table 1-3. CRT-D and OPT Cause of Death

Cause of Death	OPT Arm (N = 308)	CRT-D Arm (N = 595)	Total (N = 903)
Cardiac	58 (18.8%)	76 (12.8%)	134 (14.8%)
Vascular	0 (0.0%)	3 (0.5%)	3 (0.3%)
Non-Cardiac	11 (3.6%)	21 (3.5%)	32 (3.5%)
Unknown/ Unclassified	8 (2.6%)	5 (0.8%)	13 (1.4%)
Total Deaths	**77** (25.0%)	**105** (17.6%)	**182** (20.2%)

NOTE: *After the study was stopped in November 2002, follow-up for safety continued for approximately one more year on 151 OPT and 449 CRT-D patients with the final data cut-off on November 26, 2003. During this post-trial follow-up period, an additional 54 deaths were reported, consisting of 14/151 (9.3%) OPT patients and 40/449 (8.9%) CRT-D patients.*

The mortality rates are approximately equal during this post-trial follow-up period. This may be because CRT devices were made available to OPT patients. Thus, most patients were receiving the same therapy during this interval.

Potential Adverse Events

Based on the literature and CRT-D implant experience, the following alphabetical list includes potential adverse events associated with implantation of a CRT-D system:

- Acceleration of arrhythmias
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Conductor coil fracture
- Death
- Electrolyte Imbalance/Dehydration
- Elevated thresholds
- Erosion/extrusion
- Extracardiac stimulation (e.g., phrenic, diaphragm, chest wall)
- Fibrotic tissue formation (e.g., keloid formation)
- Fluid accumulation
- Formation of hematomas or cysts
- Heart block
- Inability to defibrillate or pace
- Inappropriate therapy (e.g., shocks, ATP, pacing)
- Incomplete lead connection with pulse generator
- Infection
- Lead displacement/dislodgment
- Lead fracture
- Lead insulation breakage or abrasion
- Lead tip deformation and/or breakage
- Local tissue reaction
- Muscle and nerve stimulation

- Myocardial trauma (e.g., cardiac perforation, irritability, injury)
- Myopotential sensing
- Oversensing/undersensing
- Pacemaker-mediated tachycardia
- Pericardial rub, effusion
- Pneumothorax
- Random component failures
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Thrombosis/thromboemboli
- Valve damage
- Venous occlusion
- Venous trauma (e.g., perforation, dissection, erosion)

Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychologic intolerance to an implantable system that may include the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking

In addition to the implantation of an ICD system, potential adverse events associated with implantation of a coronary venous lead system are listed below in alphabetical order:

- Allergic reaction to contrast media
- Breakage/failure of implant tools
- Coronary venous occlusion
- Coronary venous trauma (e.g., perforation, dissection, erosion)
- Prolonged exposure to fluoroscopic radiation
- Renal failure from contrast media used to visualize coronary veins

CLINICAL STUDIES

Clinical Study Populations

Guidant CRT-Ds, when compared to OPT alone, have been demonstrated with reasonable assurance, to be safe and effective in significantly reducing: the risk of a composite of all-cause mortality or first hospitalization by 20%, the risk of all-cause mortality by 36%, and heart failure symptoms in patients who have moderate to severe heart failure (NYHA III/IV) including left ventricular dysfunction (EF $\leq$ 35%) and QRS duration $\geq$ 120 ms and remain symptomatic despite stable, optimal heart failure drug therapy, based on the Guidant sponsored COMPANION clinical study. (Guidant devices were the only devices studied in the COMPANION clinical trial.)

Clinical Study Summaries

COMPANION

The COMPANION clinical study was designed to determine whether combined all-cause mortality or first hospitalization in heart failure patients receiving optimal pharmacologic therapy (OPT) can be reduced by combining OPT and 1) biventricular pacing therapy alone (CRT-P) or 2) biventricular pacing with defibrillation (CRT-D). All-cause mortality or first hospitalization (time to first event) analyzed from the time of randomization, was the primary endpoint of the study.

Guidant conducted the COMPANION study in part to demonstrate the safety and effectiveness of Guidant CRT-D and CRT-P devices in the COMPANION patient population. Trial objectives included establishing that OPT combined with biventricular pacing with defibrillation [CONTAK CD] is superior to OPT alone in improving exercise performance (Sub-study), reducing combined all-cause mortality or first hospitalization (Primary endpoint), reducing cardiac morbidity (Secondary endpoint) and reducing all-cause mortality (Secondary endpoint).

The COMPANION trial utilized a Steering Committee, Data Safety Monitoring Board (DSMB), and Morbidity and Mortality Committee for study conduct, safety, and event adjudication respectively.

The clinical study began January 20, 2000 and was conducted at 128 centers within the United States.

The COMPANION clinical study was monitored using a sequential design and on November 18, 2002, after review of the data by the Data Safety and Monitoring

Board, enrollment in the study was stopped. The CRT-D arm of the trial had reached the target number of events for the combined primary all-cause mortality or first hospitalization endpoint, as well as the secondary all-cause mortality endpoint. All effectiveness follow-ups ended by December 1, 2002.

CONTAK CD

Guidant conducted the CONTAK CD Study to demonstrate the safety and effectiveness of the CONTAK CD system and to demonstrate a reasonable assurance of the safety and effectiveness of biventricular stimulation, or cardiac resynchronization therapy (CRT), using the Guidant Model 1822 VENTAK CHF AICD and Model 1823 CONTAK CD CRT-D along with the EASYTRAK (Models 4510/4511/4512/4513) coronary venous, steroid-eluting, single-electrode pace/sense lead.

The CONTAK CD Study failed to prospectively demonstrate effectiveness of the CRT portion of the device. The CONTAK CD Study met the Lead and System Effectiveness endpoints as well as the Lead and System Safety endpoints. Subgroup analysis revealed a population of patients that had Class III/IV heart failure at the time of randomization that appeared to have improvements on certain functional endpoints, including the Peak VO_2 and the Six-Minute Hall walk. A second study was performed (Focused Confirmatory Study) using this subgroup of patients to confirm the effectiveness of CRT.

CONTAK RENEWAL

Guidant also conducted the CONTAK RENEWAL Study, which demonstrated the device's ability to appropriately detect ventricular tachyarrhythmias with an independent sensing configuration. Finally, the CONTAK RENEWAL Holter Study was conducted to provide confirmation of the device's ability to provide continuous biventricular pacing on both a daily basis and during exercise.

COMPANION Study

The COMPANION study design and study results have been previously described in the medical literature.[3,4]

3. Bristow MR, Feldman AM, Saxon LA. Heart failure management using implantable devices for ventricular resynchronization: Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial. J Card Fail. 2000;6(3):276-285.
4. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140-2150.

Study Design

The COMPANION study was a prospective, randomized [1:2:2 to OPT, CRT-P (delivered by the CONTAK TR device), or CRT-D (delivered by the CONTAK CD device)], controlled, multi-center study. Both of these devices became commercially available during the course of the study.

Randomization was stratified by centers and by beta-blocker use to assure proper balance between the treatment groups within each center. Each randomized patient remained counted as a member of the original randomization assignment (intention-to-treat) regardless of subsequent crossover or protocol adherence.

Eligible patients were also enrolled in a sub-study designed to measure improvement in exercise performance in patients randomized to CRT (CRT-P and CRT-D pooled data) therapy compared to OPT.

Endpoints

This summary focuses on the CRT-D vs. OPT contrast, providing evidence of safety and effectiveness for Guidant CRT-Ds in the COMPANION patient population[5]. The clinical data and analyses herein address the following study endpoints for all patients randomized to CRT-D and OPT only, unless otherwise stated as a sub-study measurement (where CRT-D and CRT-P data were pooled for exercise performance):

Primary Endpoint

The primary endpoint was a composite consisting of all-cause mortality or first hospitalization (time to first event) as analyzed from the date of randomization on an intention-to-treat basis. The study was designed to demonstrate a 25% relative reduction with CRT-D when compared to an estimated 40% annual rate in the OPT cohort. All-cause mortality was defined as death from any cause. Hospitalization is defined below:

Qualifying Duration for Hospitalization

The intent behind hospitalization was to capture hospitalizations that were of sufficient duration to enter into a composite with all-cause mortality. Thus, hospitalization was defined as care provided at a hospital in which hospital

5. Guidant CRT-Ps are already approved for use in the COMPANION patient population, P030005, approved 01/26/04.

admission and discharge occurred on separate dates. Patients excluded from this definition were those who received care at a hospital, but were discharged on the same day as admission. In addition to hospitalizations, the use of intravenous inotropes or vasoactive agents for a duration of greater than four hours was also considered to be of significant importance to be treated as an instance of hospitalization.

Hospitalizations Related to the Implant Procedure

Hospitalizations associated with device implant (initial and reattempted for unsuccessful initial implant) were not considered to be an event for evaluating the primary endpoint. Similarly, hospitalizations associated with elective implant of devices (i.e., absence of an electrophysiological indication or an ongoing hospitalization requiring intravenous therapy) in the OPT cohort also were not considered to be a primary endpoint event. Surgical revisions of a previous implanted system did count as a primary endpoint event if the revision was of a sufficient duration to result in different admission and discharge dates. Table 1-4 summarizes the criteria for determining which hospitalization events were considered as a primary endpoint event.

Table 1-4. Hospitalizations Contributing to Primary Endpoint

Event Description	CRT-D	OPT
Initial implant/reattempts	No	No
Surgical revisions of system	Yes[a]	Yes[a]
Hospitalization with no calendar date change	No	No
Hospitalization with a calendar date change	Yes	Yes
IV inotrope and/or vasoactive drug use > 4 hours	Yes	Yes

a. If calendar date change.

Secondary Endpoints

All-cause mortality: The all-cause mortality (death from any cause) endpoint was designed to show a 25% reduction in mortality in the CRT-D arm from an OPT annual mortality rate of 24%. Difference in mortality was determined by contrasting patients randomized to CRT-D in addition to OPT versus patients randomized to OPT alone.

Cardiac morbidity: The hospitalization component of the primary endpoint included non-cardiac events that may not be impacted by CRT-D. The cardiac morbidity endpoint was unique to the COMPANION study. It is a more specific outcome measure intended to determine whether CRT-D when compared to OPT would reduce the type of events that are pertinent to a hospitalization for heart failure.

Cardiac morbidity was defined as the occurrence of one or more of the following events:

- Worsening heart failure resulting in use of intravenous vasoactive or inotropic therapy exceeding four hours
- Mechanical respiratory or cardiac support
- Any cardiac surgery, including heart transplant
- Resuscitated cardiac arrest or sustained ventricular tachycardia requiring intervention (e.g., chest thump, external cardioversion, or external defibrillation)
- Hospitalization for acute decompensation of heart failure
- Hospitalization that results in death from cardiac causes
- Significant device-related events resulting in:
    - Permanent disability
    - Hospitalization for pending death or permanent disability

Safety

CRT-D system-related complication-free rate is determined by measuring complications related to any of the implanted components or their associated implant procedure in those patients who were successfully implanted with the CRT-D system.

NOTE: *During the course of the COMPANION clinical study, the EASYTRAK Coronary Venous pace/sense lead was established as safe and effective in a separate clinical study and was approved for commercial distribution (P010012, 05/02/02). Refer to the commercially available EASYTRAK Coronary Venous pace/sense lead labeling for clinical safety and performance characteristics.*

Sub-study Primary Endpoint and Additional Tertiary Endpoints

Exercise performance: The co-primary endpoint, which consists of Peak VO_2 and Six-Minute Walk, is designed to demonstrate improvement in exercise performance with CRT (CONTAK TR and CONTAK CD pooled data) compared to OPT at six months post-baseline.

Additional tertiary endpoints included Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire© and NYHA Class.

Inclusion Criteria

The study population consisted of patients with moderate to severe heart failure, New York Heart Association Classification III or IV, left ventricular ejection fraction ≤ 35%, and QRS width ≥ 120 ms due to ischemic or non-ischemic cardiomyopathy.

All patients were required to have been treated with a stable dose of beta-blocker, ACE inhibitor or ARB, diuretic, and aldosterone antagonist. A stable dose was defined as 30 days for all drugs except beta-blocker, which required 90 days stabilization from last up titration prior to randomization. Diuretic dosage could be adjusted any time by the investigator using medical discretion.

Patients enrolled in the study were required to meet the following inclusion criteria:

- Moderate or severe heart failure, defined as symptomatic heart failure for at least six months with NYHA class III or IV symptoms at the time of enrollment, and at least one of the following events in the previous 12 months:
  - — Hospitalization for heart failure management
  - — Outpatient visit in which intravenous (IV) inotropes or vasoactive infusion were administered continuously for at least 4 hours
- QRS ≥ 120 ms and PR interval > 150 ms from any two leads of a 12 lead ECG
- Left ventricular ejection fraction ≤ 35%
- Left ventricular end diastolic dimension ≥ 60 mm (required only if LVEF measured by echo) or > 3.0 cm/m^2 [The cm/m^2 is calculated by LVEDD (in cm) divided by BSA (body surface area)]

- Emergency room visit of at least twelve hours duration in which IV heart failure medications were administered (including diuretics)

- Age ≥ 18 years
- Optimal pharmacologic therapy for heart failure (beta-blocker, ACE inhibitor, diuretics, and spironolactone)

Additional eligibility criteria for the Exercise Performance sub-study:

- Understand the nature of the sub-study and provide informed consent
- Have been enrolled at a participating sub-study investigational center
- Have no neuromuscular or vascular disability that prevents normal walking (e.g., intermittent claudication, arthritis, residual stroke weakness)
- Have no history of angina during previous exercise testing
- $FEV_1/FVC \geq 50\%$
- 150 m ≤ Six minute walk distance ≤ 425 m
- Baseline Peak $VO_2 < 22$ ml/kg/min
- Have no cardiac disabilities that would ordinarily contraindicate exercise testing:
  - changing pattern on the ECG
  - changing pattern of chest discomfort
  - decompensated heart failure
  - uncontrolled arrhythmias

Exclusion Criteria

Patients were excluded from the investigation if they met any of the following criteria:

- Unable or unwilling to undergo device implant and follow-up testing
- Patients with a hypersensitivity to 0.7 mg nominal dose of dexamethasone acetate

- Meet the general indications for an implantable cardioverter defibrillator
- Meet the general indications for antibradycardia pacing
- Expected to receive a heart transplant in the next six months
- Chronic, medically refractory atrial tachyarrhythmias
- Unexplained syncope
- Myocardial infarction within 60 days of randomization
- History of non-compliance with oral heart failure therapy
- Progressive or unstable angina
- Uncontrolled blood pressure: Systolic BP > 160 mm Hg or < 85 mm Hg or diastolic BP > 90 mm Hg
- Surgically uncorrected primary valvular disease
- Coronary artery disease (CAD) in which surgical or percutaneous correction is recent (within 60 days of randomization)
- Women who are pregnant or not using medically acceptable birth control
- Hypertrophic obstructive cardiomyopathy
- Amyloid disease
- Hospitalization for heart failure or IV inotropic or vasoactive therapy in excess of 4 hours in the 30 days prior to enrollment
- Involved in any other investigational studies
- Life expectancy < 6 months due to any other medical conditions

Follow-up Schedule

Enrollment	Initial assessment of patient eligibility; taking of patient history.
Baseline Screening	Special testing[a]
Randomization	Randomization status (OPT, CRT-P, or CRT-D) was assigned.
Implant (CRT-P or CRT-D arm)	Implant of investigational devices and acute device testing for those randomized to a CRT therapy arm.
Routine Follow-up	Routine evaluation of device function and patient condition at pre-discharge, one week, and one month.

Three- and six-month Visits	Evaluation of randomized therapy with Special Testing[a] and device function at three and six months after the Post-Recovery Visit.
Quarterly Visits	After the six-month visit, patients were seen for routine evaluation of device function and patient condition.

a. Special Testing included a Symptom-Limited Treadmill Test with measurement of oxygen uptake (Peak VO_2), a Six-Minute Walk, Quality of Life (QOL) questionnaire and New York Heart Association Classification.

Demographic Data

All baseline patient characteristics are presented in Table 1-5.

Table 1-5. Characteristics of Patient Population for COMPANION (OPT and CRT-D)

Characteristic		OPT (N = 308)	CRT-D (N = 595)	P-value
Age (years)	Mean ± SD	66.7 ± 10.7	65.6 ± 11.2	0.14
Gender [N (%)]	Female	97 (31.4)	194 (32.6)	0.73
	Male	211 (68.5)	401 (67.3)	
NYHA Classification [N (%)]	Class III	253 (82.1)	512 (86.1)	0.12
	Class IV	55 (17.8)	83 (13.9)	
Ischemic Etiology (%)	Ischemic	58.7	54.6	0.13
	Non-ischemic	41.3	45.4	
LVEF (%)	Mean ± SD	22.8 ± 7.2	22.5 ± 6.8	0.47
Resting Heart Rate (bpm)	Mean ± SD	72 ± 12	73 ± 13	0.37
QRS Width (ms)	Mean ± SD	156 ± 24	159 ± 24	0.09
Conduction Abnormality (%)	LBBB	69.8	72.9	0.21
	Non-specific	21.4	16.8	
	RBBB	8.77	10.2	
Duration of Heart Failure (years)	Mean ± SD	4.86 ± 4.41	4.44 ± 3.83	0.43

Table 1-5. Characteristics of Patient Population for COMPANION (OPT and CRT-D)

Characteristic		OPT (N = 308)	CRT-D (N = 595)	P-value
Heart Failure Medications [(%)]	Diuretic	94.4	96.6	0.12
	ACE inhibitor or ARB	88.6	89.6	0.66
	Beta Blockers	66.2	67.6	0.69
	Aldosterone Antagonist	54.8	55.1	0.94
	Digoxin	67.2	70.9	0.25

Patient Accountability and Follow-up Duration

The COMPANION study enrolled 1638 patients, with 1520 patients randomized to a treatment group and one hundred eighteen patients (118) not randomized due to changes in patient condition or consent between time of enrollment and time of randomization, such that the inclusion criteria were no longer satisfied. Of the 1520 patients, 595 were randomized to CRT-D with a mean follow-up of 1.3 years and 308 were randomized to OPT with a mean follow-up of 1.1 years. Figure 1-1 provides an overview of patient enrollment.

Table 1-6 gives a summary (by treatment group) of patient disposition over time through 12 months after randomization. This does not account for patients that had a hospitalization or death event that contributed to the primary endpoint or secondary endpoint of all-cause mortality. For events contributing to the primary endpoint or the secondary endpoint of all-cause mortality, please refer to Figure 1-2 on page 1-33 and Figure 1-3 on page 1-34.

Table 1-6. Patient Follow-up Disposition 12 Months Post Randomization

	CRT-D				OPT			
	# of With-drawn Patients	# of Deceased Patients	(N = 595) # Reached end of study (Nov. 30, 2002)	# of Active Patients at end of time interval	# of With-drawn Patients	# of Deceased Patients	(N = 308) # Reached end of study (Nov. 30, 2002)	# of Active Patients at end of time interval
1 Day - 7 Days	4	3	0	588	6	0	0	302
7 Days - 1 Month	4	3	5	576	10	3	1	288
1 Month - 3 Months	4	15	6	551	11	11	1	265
3 Months - 9 Months	12	28	49	462	26	22	29	188
9 Months - 12 Months	1	12	35	414	11	11	19	147

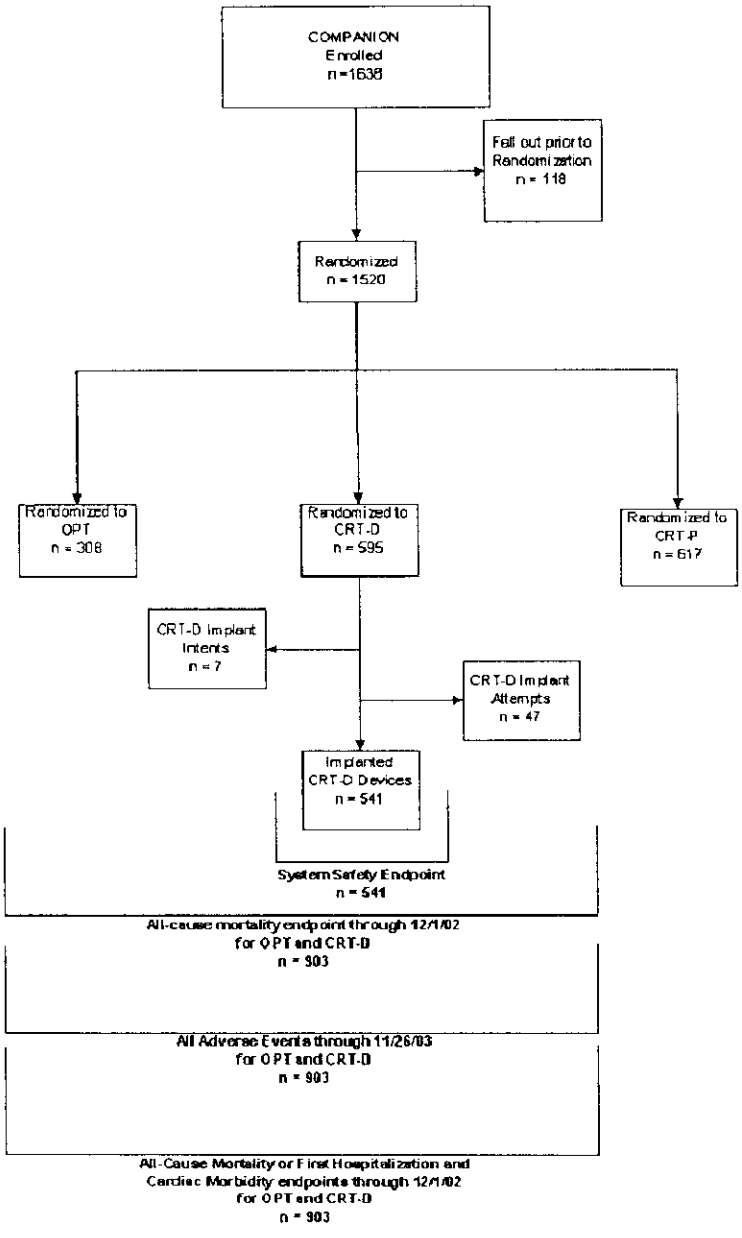

Figure 1-1. Study Patient Enrollment and Randomization for CRT-D and OPT.

Event Contributing to Primary Endpoint and Secondary Endpoint of All-cause Mortality

A total of 903 COMPANION patients in the CRT-D (595) and OPT (308) groups were eligible for the primary endpoint. Figure 1-2 provides patient randomization and status for the primary endpoint and Figure 1-3 provides patient randomization and status for the secondary mortality endpoint.

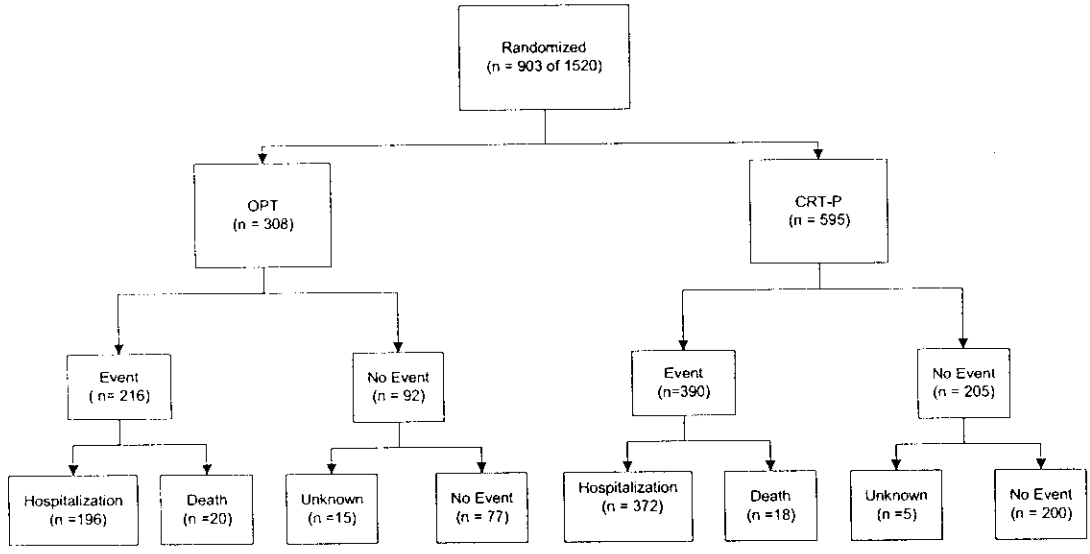

Figure 1-2. CRT-D and OPT Patient Randomization for Primary Endpoint.

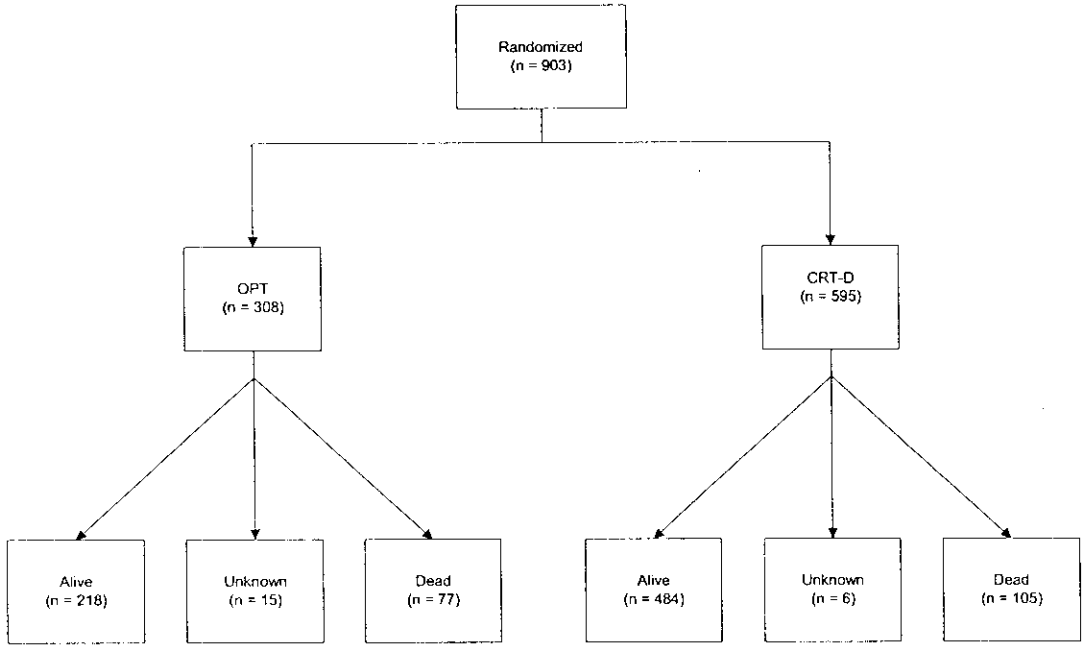

Figure 1-3. CRT-D and OPT Patient Randomization for Mortality Endpoint.

Data Analysis and Results for Primary Endpoint and Secondary All-Cause Mortality Endpoint

Sequential Monitoring

The COMPANION DSMB met approximately every six months to review the trial's progress and to review the safety and effectiveness data collected. An "O'Brien-Fleming" type boundary as implemented by Lan and DeMets was used in monitoring the trial. The Group sequential procedure ensured that the total alpha spent across repeated analyses did not exceed the total type I error, in this case $\alpha = 0.03$.

On November 18, 2002 the DSMB reviewed the study progress for the final time. The CRT-D arm of the Study had reached the target number of events for both the combined mortality and hospitalization endpoint as well as the all-cause mortality

endpoint prompting the DSMB to recommend to the Steering Committee that enrollment be stopped. All effectiveness follow-ups ended on December 1, 2002.

RESULTS

Primary Endpoint: All-cause Mortality or First Hospitalization

The Kaplan-Meier curves illustrating the time to all-cause mortality or first hospitalization are shown in Figure 1-4. There were 216 primary endpoint events observed in the OPT arm and 390 in the CRT-D arm ($p = 0.010$; $p = 0.011$ after adjustment for interim analyses). The median time to first event was 209 days in the OPT group and 269 days in the CRT-D group. The annual event rates for OPT and CRT-D, respectively, were 68.0% and 55.9%, with a hazard ratio of 0.80; 95% CI (0.68, 0.95). This result demonstrated that CRT-D significantly reduced the relative risk of all-cause mortality or first hospitalization by 20% when compared to OPT alone.

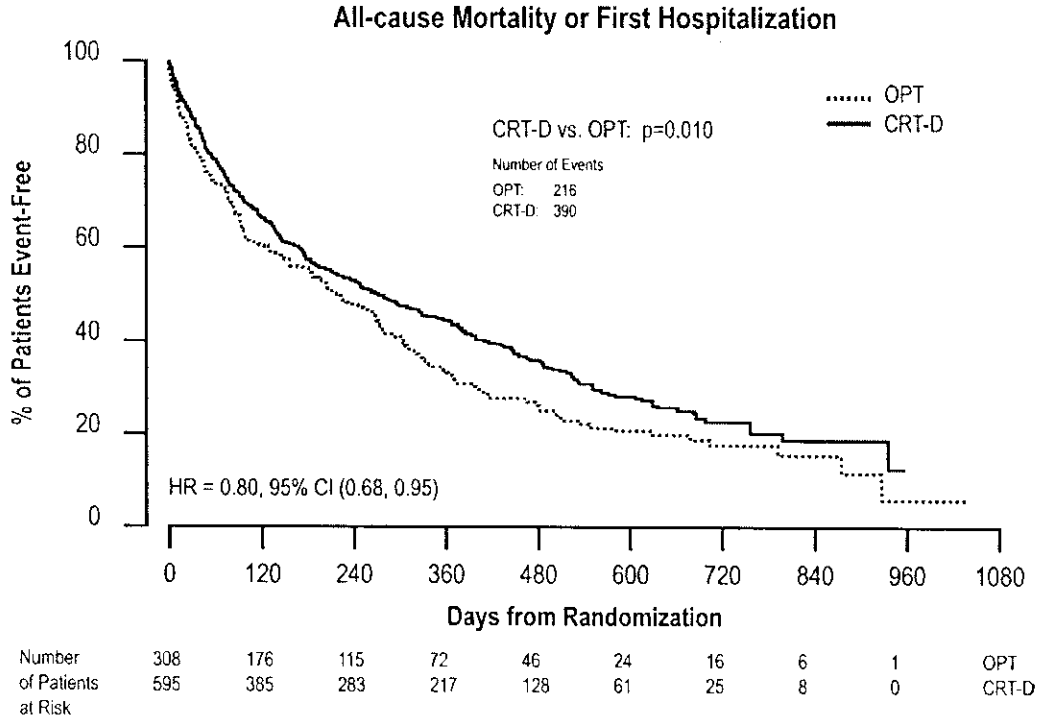

Figure 1-4. Primary Endpoint: All-cause Mortality or First Hospitalization.

In addition to the hazard ratio, point estimates of risk reduction were also calculated (Table 1-7). These estimates will vary with time from the true treatment effect, and thus should be interpreted with caution.

Table 1-7. Primary Endpoint Risk Reduction Point Estimates (Overall Hazard Ratio = 0.80; p = 0.010)

	% Failure		Absolute Risk Reduction	Relative Risk Reduction
	OPT	CRT-D		
6 months	44.9% (38.9%, 50.3%)	42.9%(38.7%, 46.7%)	2.0%	4.5%

Table 1-7. Primary Endpoint Risk Reduction Point Estimates (Overall Hazard Ratio = 0.80; p = 0.010)

	% Failure		Absolute Risk Reduction	Relative Risk Reduction
	OPT	CRT-D		
12 months	68.0% (61.7%, 73.2%)	55.9% (51.6%, 59.8%)	12.1%	17.8%
18 months	77.8% (71.6%, 82.7%)	69.0% (64.5%, 73.1%)	8.8%	11.3%

Secondary Endpoints

All-cause Mortality

Deaths from any cause were reported in 77 patients randomized to OPT and 105 patients randomized to CRT-D (p = 0.003, p = 0.004 after adjusting for interim analyses). The Kaplan-Meier curves are depicted in Figure 1-5. These numbers correspond to an annual mortality rate of 19% in the OPT arm and 12% in the CRT-D arm, with a hazard ratio of 0.64, 95% CI (0.48, 0.86). These results demonstrated that CRT-D was associated with a 36% reduction in the risk of all-cause mortality when compared to OPT alone.

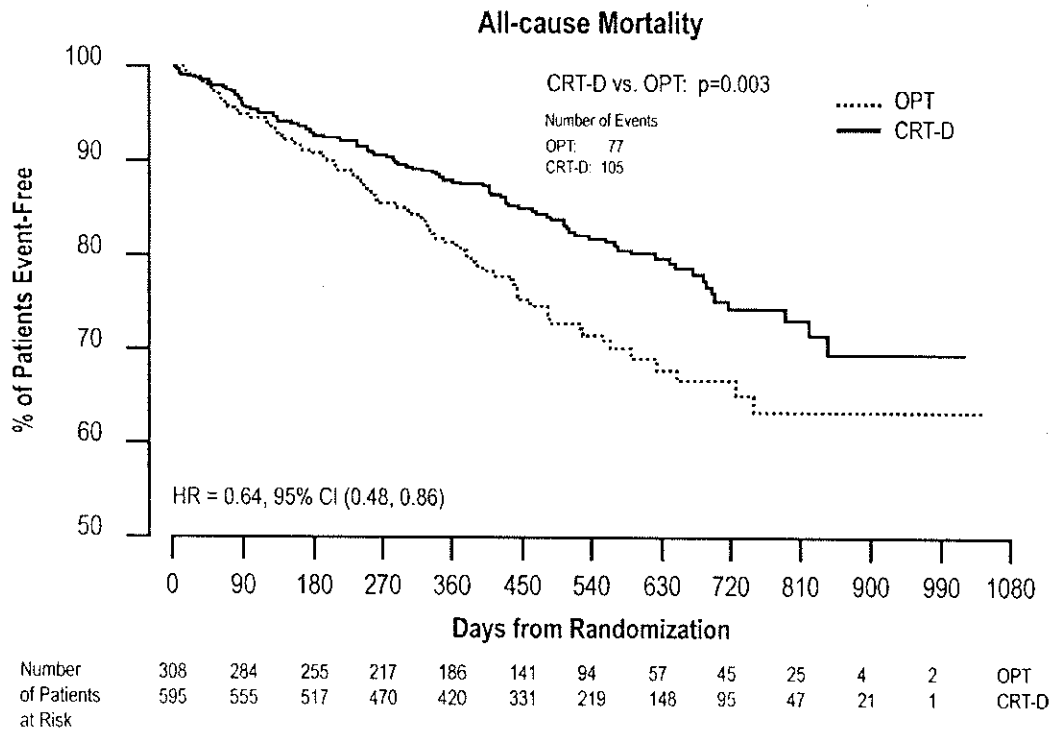

Figure 1-5. Secondary Endpoint: All-cause Mortality.

In addition to the hazard ratio, point estimates of risk reduction were also calculated (Table 1-8). These estimates will vary with time from the true treatment effect, and thus should be interpreted with caution.

Table 1-8. Mortality Endpoint Risk Reduction Point Estimates (Overall Hazard Ratio = 0.64; p = 0.003)

	% Failure		Absolute Risk Reduction	Relative Risk Reduction
	OPT	CRT-D		
6 months	9.0% (5.7%, 12.2%)	7.3% (5.1%, 9.3%)	1.7%	18.9%
12 months	18.9% (14.1%, 23.5%)	12.1% (9.3%, 14.8%)	6.8%	36.0%

Table 1-8. Mortality Endpoint Risk Reduction Point Estimates (Overall Hazard Ratio = 0.64; p = 0.003)

	% Failure		Absolute Risk Reduction	Relative Risk Reduction
	OPT	CRT-D		
18 months	28.4% (22.3%, 34.1%)	18.0% (14.4%, 21.5%)	10.4%	36.6%

Results for Secondary Cardiac Morbidity Endpoint

As previously mentioned in the Cardiac Morbidity section on page 1-25, cardiac morbid events were reported during hospitalizations.

During a hospitalization more than one of the pre-specified cardiac morbid events could occur. The Anderson-Gill extension to the Cox proportional hazard model was used to analyze time to multiple cardiac morbid events. Caution must be used in interpreting p-values in this analysis because this analysis does not account for the competing risk of death.

In Figure 1-6, the frequency and duration of cardiac morbid events are illustrated. CRT-D was associated with a 36% reduction ($p < 0.0001$) in the proportion of patients with at least one event, a 52% reduction ($p < 0.0001$) in events on an annual basis, and a 41% reduction ($p < 0.0001$) in the hospital duration on an annual basis. These reductions are primarily due to the reduction of hospitalizations for acute decompensation of heart failure, worsening heart failure resulting in IV inotrope or vasoactive therapy > 4 hours (during an inpatient hospitalization) and cardiac surgery (including percutaneous intervention), as shown in Figure 1-7.

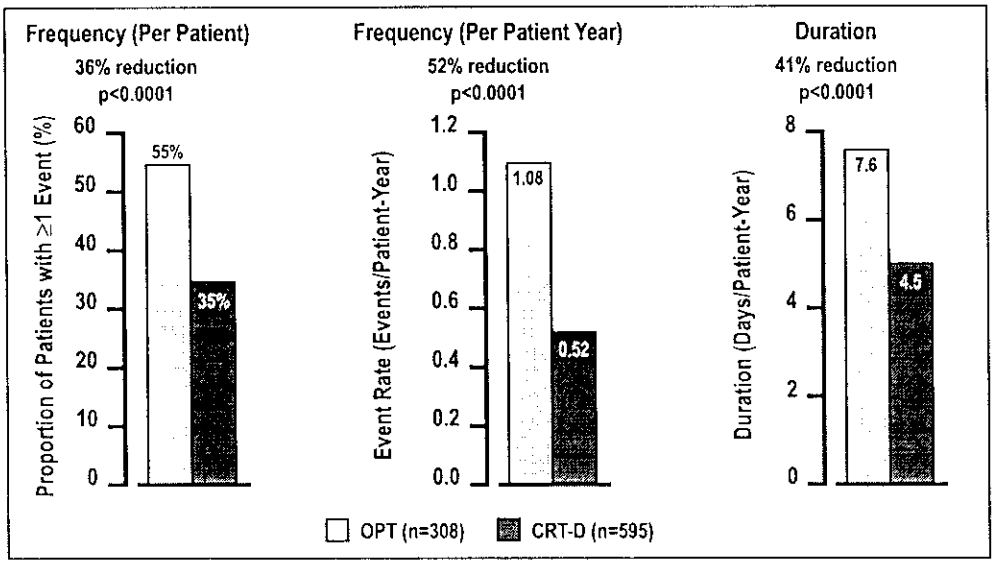

Figure 1-6. Secondary Endpoint of Cardiac Morbidity.

Caution must be used in interpreting p-values; analysis does not account for competing risk of death.

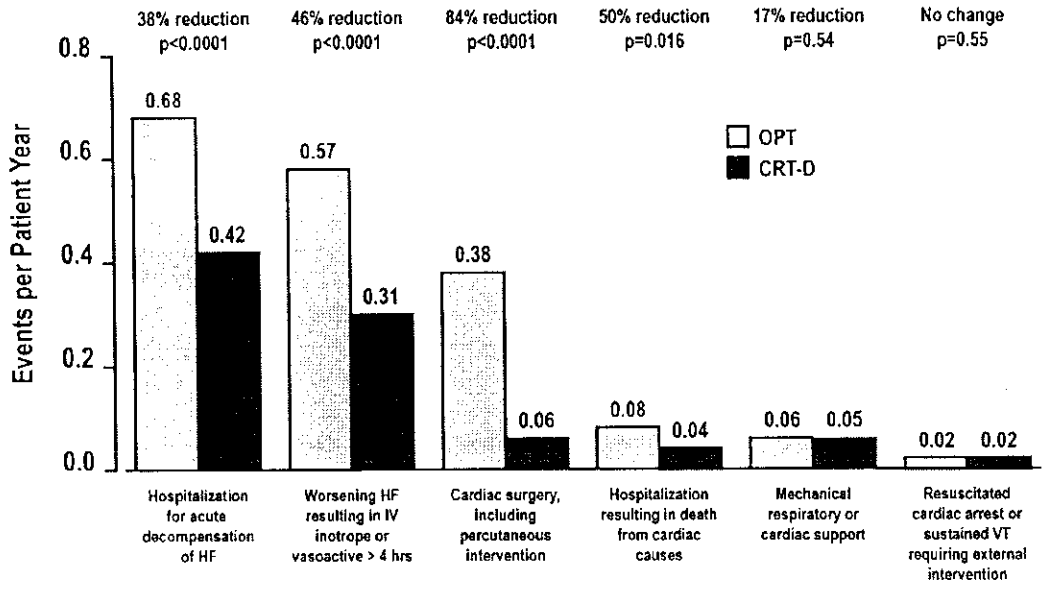

Figure 1-7. Cardiac Morbidity by Major Component.

For a given cardiac hospitalization, patients may have events in more than one category, and if there are multiple occurrences in a single category, then only the first occurrence was counted.

Other Analyses

Implant Disposition

Table 1-9 identifies the number of initial and subsequent implant procedures attempted in patients randomized to CRT-D and the rate of success for each additional implant procedure. There were 81 CRT-D patients that had an unsuccessful initial implant for the CRT-D system. Fifty (50) of these patients had a second implant procedure, of which 33 were successful and 17 were unsuccessful. Three patients had a third implant procedure, of which one was successful. Therefore, there were 541 patients implanted with the CRT-D system.

Table 1-9. CRT-D System Implant Disposition

		Attempt successful	Failed implant	Reattempt not done after this procedure
Initial implants	588 (98.8%)	507 (85.0%)	81 (14.0%)	31 (5.2%)
First reattempt	50 (8.4%)	33 (5.5%)	17 (2.9%)	14 (2.3%)
Second reattempt	3 (0.5%)	1 (0.2%)	2 (0.3%)	2 (0.34%)

Additional Outcome Measures

First Heart Failure Hospitalizations

An additional outcome that was not pre-specified in the protocol provides further insight into the results observed in the composite primary endpoint. This post-hoc analysis was conducted using cause-specific hospitalizations as adjudicated by the morbidity and mortality committee and therefore should be interpreted with caution.

The outcome of all-cause mortality or first heart failure hospitalization was analyzed on an intention-to-treat basis and time to first event.

Hospitalizations were defined per the following:

- Care provided at a hospital for any reason in which the duration is associated with a date change, or
- Use of intravenous inotropes and/or vasoactive drugs for a duration > 4 hours (inpatient or outpatient).

NOTE: *Hospitalizations associated with a device implant attempt or re-attempt are excluded.*

Those contributing to the heart failure hospitalization outcome were required by the Morbidity and Mortality committee to meet at least one of the following additional criteria:

- IV diuretics
- IV inotrope/vasoactive therapy

- Other parenteral therapy for the treatment of heart failure
- Significant alterations in oral therapy for the treatment of heart failure

All-cause Mortality or First Heart Failure Hospitalization

The Kaplan-Meier curves for all-cause mortality or first heart failure hospitalization is shown in Figure 1-8. OPT and CRT-D had annual event rates of 45% and 29%, respectively with a hazard ratio of 0.60, 95% CI (0.49-0.75), $p < 0.001$. Therefore, CRT-D was associated with a 40% relative reduction in the risk of all-cause mortality or first heart-failure hospitalization when compared to OPT alone.

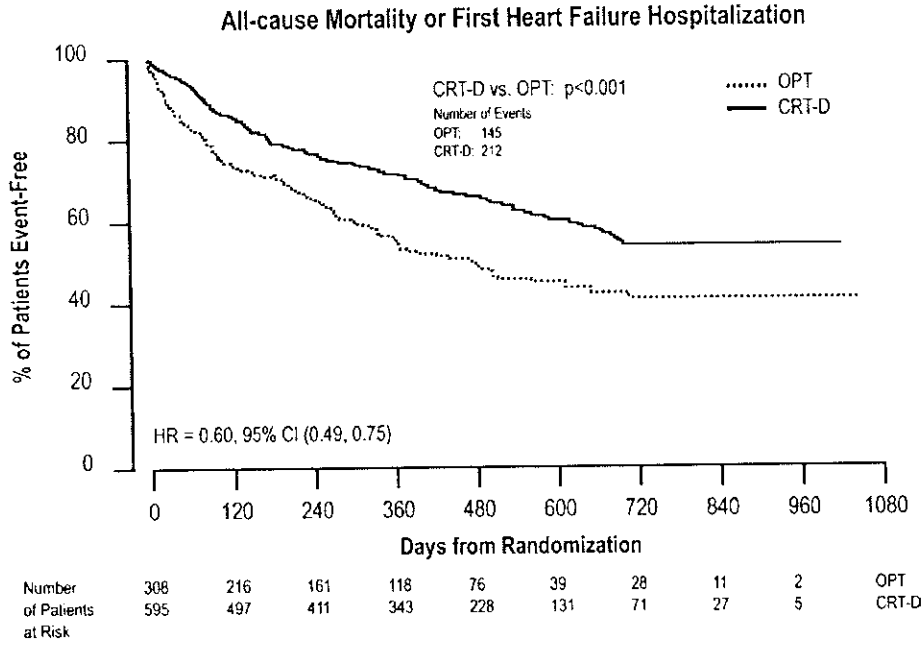

Figure 1-8. Additional Outcome: All-cause Mortality or First Heart Failure Hospitalization.

Disposition of Hospitalization

Implantation of the CRT-D system generally requires hospitalization. To differentiate between the hospitalization required to implant the system and those hospitalizations that occurred after the system was implanted, the following terms are used:

- Implant hospitalization: The elective hospitalization associated with either the implant procedure or a repeat implant procedure if the initial procedure was unsuccessful.

- All other hospitalizations: Patients who required a revision for an implanted system (e.g., lead dislodgment or infection) were included in this category as were hospitalizations for non-elective device related implants.

The hospitalizations analysis illustrated in Figure 1-9 and hospitalization days analysis in Figure 1-10 depicts hospitalization data stratified by *implant* and *non-elective hospitalizations*. This analysis was on an intention-to-treat basis and includes patients who underwent an attempted implant procedure. Patients randomized to CRT-D had a follow-up duration approximately 30% longer than OPT patients. Thus, hospitalization data are normalized per patient-year of follow-up. An additional comparison of hospitalization days for heart failure hospitalizations are shown in Figure 1-11.

NOTE: *CRT-D was associated with a reduction in all-cause mortality and therefore there is a competing risk for hospitalizations. This data should be interpreted with caution.*

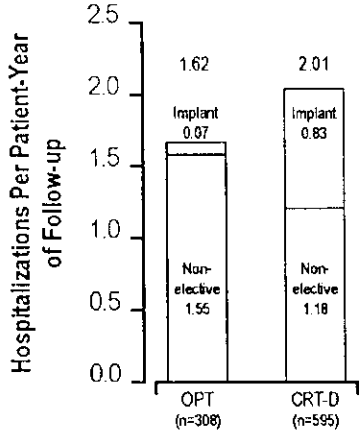

Figure 1-9. Hospitalizations/Patient year.

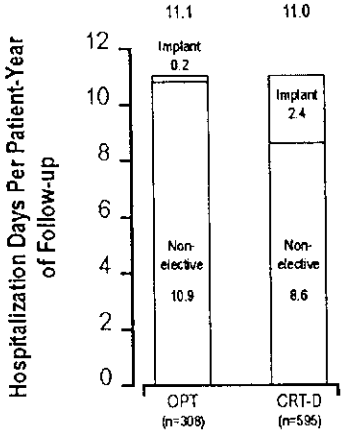

Figure 1-10. Hospitalization Days/Patient-Year: Hospitalizations.

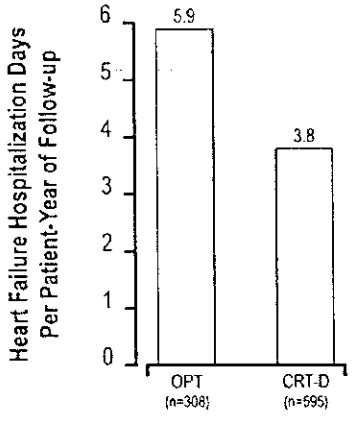

Figure 1-11. Hospitalization Days/Patient-Year: Heart Failure Hospitalizations.

Data Analysis and Results: CRT-D System Safety

The system-related complication-free rate analysis was not a predefined endpoint in the protocol. The intent of this analysis is to provide reasonable assurance of safety of the CONTAK CD system in this patient population. The system-related complication-free rate was defined over a six-month follow-up period as the proportion of patients who are free of complications attributed to:

- Any implanted component (e.g, pulse generator, coronary venous lead, right atrial pace/sense lead, cardioversion/defibrillation lead)

- The surgical procedure required to implant the CRT-D system

In the COMPANION study, this analysis was performed on an intention-to-treat basis and also extends to those patients who underwent an implant procedure but did not ultimately receive a device. Of the 595 patients analyzed, 522 (87.7%) were free of system-related complications.

Of the 73 (12.3%) patients who experienced a system-related complication, the most common were loss of left ventricular capture (25 patients, 4.2%), loss of right atrial capture (9 patients, 1.5%), and phrenic nerve/diaphragmatic stimulation (8 patients, 1.3%).

When analyzed on a time-to-event basis, the system-related complication-free rate was 87.7%. The safety performance of the CONTAK CD system compares favorably with the safety performance observed in the prior CONTAK CD study (P010012, May 2, 2002).

Data Analysis and Results for COMPANION Sub-study

The Exercise Performance Sub-study consisted of:

CRT Effectiveness:

Primary: Co-primary endpoint consisting of Peak VO_2 derived from a symptom-limited exercise test and Six-Minute Walk, with CRT results pooled from the CONTAK TR and CONTAK CD arms.

Effectiveness was determined by assessing both Peak VO_2 and Six-Minute Walk distance improvements with CRT compared to OPT. Prospectively, success was defined as occurring if:

- Peak VO_2 improved ≥ 0.7 ml/kg/min ($p < 0.05$) and 6 MWD improvement resulted in $p < 0.10$, or

- Peak VO_2 improved ≥ 0.5 ml/kg/min ($p < 0.10$) and 6 MWD improvement resulted in $p < 0.05$.

Additional: Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire® and NYHA Class.

Patient Accountability

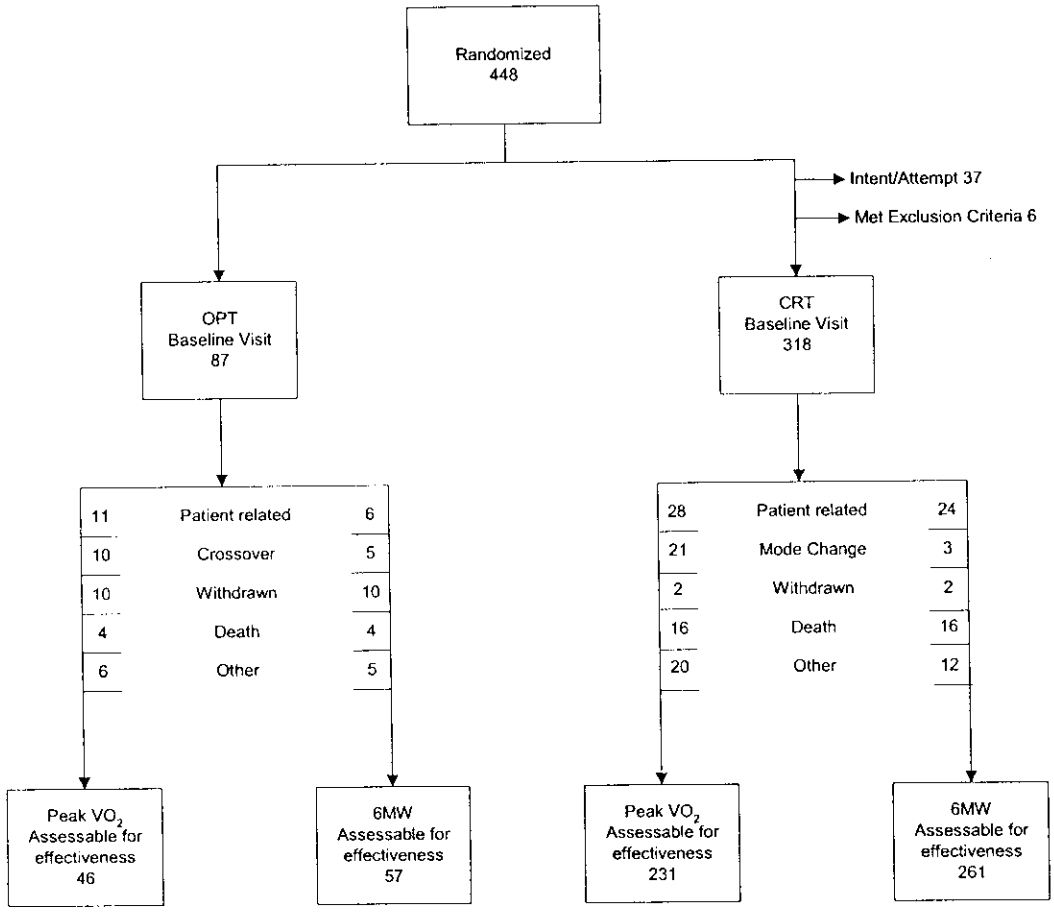

Figure 1-12. Enrollment and Follow-up of Randomized Patients.

Baseline Characteristics

Table 1-10. Characteristics of Patient Population

Characteristic		CRT (N = 318)	OPT (N = 87)	P-value[a]
Age (years)	Mean ± SD	62.1 ± 11.8	63.1 ± 10.6	0.48
	Range	32.0–86.0	27.0–85.0	
Gender [N (%)]	Female	109 (34.3)	24 (27.6)	0.24
	Male	209 (65.7)	63 (72.4)	
NYHA Classification [N (%)]	III	294 (92.5)	79 (90.8)	0.61
	IV	24 (7.5)	8 (9.2)	
Ischemic Etiology	Ischemic	141 (44.3)	42 (48.3)	0.51
	Non-ischemic	177 (55.7)	45 (51.7)	
LVEF (%)	Mean ± SD	22.5 ± 6.9	22.2 ± 8.0	0.79
	Range	5.0–35.0	5.0–35.0	
Resting Heart Rate (bpm)	Mean ± SD	73.1 ± 12.8	73.5 ± 11.5	0.78
	Range	46.0–122.0	54.0–103.0	
QRS Width (ms)	Mean ± SD	159.2 ± 25.0	155.7 ± 25.8	0.26
	Range	120.0–276.0	120.0–224.0	
LBBB/NSIVCD (%)	LBBB	230 (72.3)	62 (71.3)	0.60
	Nonspecific	54 (17.0)	18 (20.7)	
	RBBB	34 (10.7)	7 (8.0)	
Peak VO_2 (ml/kg/min)	Mean ± SD	12.7 ± 3.3	12.4 ± 3.3	0.42
	Range	3.0–21.2	4.8–21.5	
Six-Minute Walk Distance (m)	Mean ± SD	292.4 ± 65.5	291.6 ± 70.5	0.92
	Range	152.0–411.5	162.4–414.0	
Quality of Life Score (points)	Mean ± SD	59.8 ± 23.1	55.4 ± 23.3	0.12
	Range	0.0–105.0	0.0–97.0	
Heart Failure Medications [N (%)]	Diuretic	300 (94.3)	82 (94.3)	0.98
	ACE Inhibitor or ARB	286 (89.9)	82 (94.3)	0.22
	Beta Blockers	240 (75.5)	60 (69.0)	0.22
	Aldosterone Antagonist	178 (56.0)	51 (58.6)	0.66
	Digoxin	239 (75.2)	65 (74.7)	0.93

a. Continuous data were analyzed using a two-tailed t-test procedure, and categorical data were analyzed using a two-tailed chi-square procedure. A p-value < 0.05 is considered significant.

CRT Effectiveness

Peak VO_2

Peak VO_2 was determined from a standardized protocol for exercise testing as a means of measuring a patient's capacity for performing physical activity.

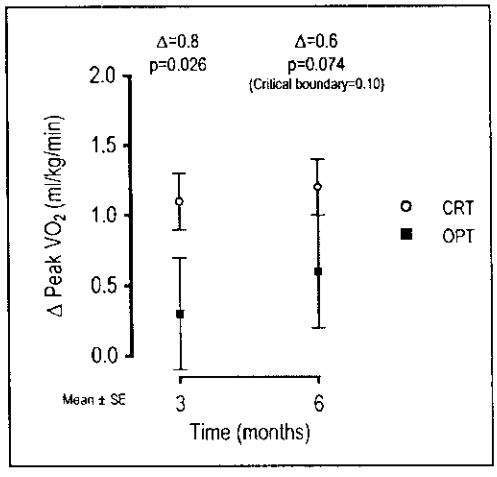

Figure 1-13. Maximal Oxygen Consumption Results.

Table 1-11. Maximal Oxygen Consumption Results

Peak VO_2 (ml/kg/min)	CRT		OPT		P-value[a]
	N	Mean ± S.E.	N	Mean ± S.E.	
Δ at 3 months	247	1.1 ± 0.2	52	0.3 ± 0.4	0.026
Δ at 6 months	230	1.2 ± 0.2	46	0.6 ± 0.4	0.074

a. P-values obtained using one-tailed longitudinal analysis methods.

The longitudinal analysis was performed on all available data. The percentages of missing data at the six-month endpoints for Peak VO_2 and Six-Minute Walk were 36 percent and 28 percent for the CRT arm and 47 percent and 34 percent for the OPT arm. The longitudinal analysis performed is most appropriate when missing data occurs at the percentages found in this trial.

Six-Minute Walk

The Six-Minute Walk test is a measure of a patient's ability to sustain exercise during an activity similar to that which a patient may typically perform on a daily basis. For this test, patients are instructed to walk as far as possible in 6 minutes in a level corridor.

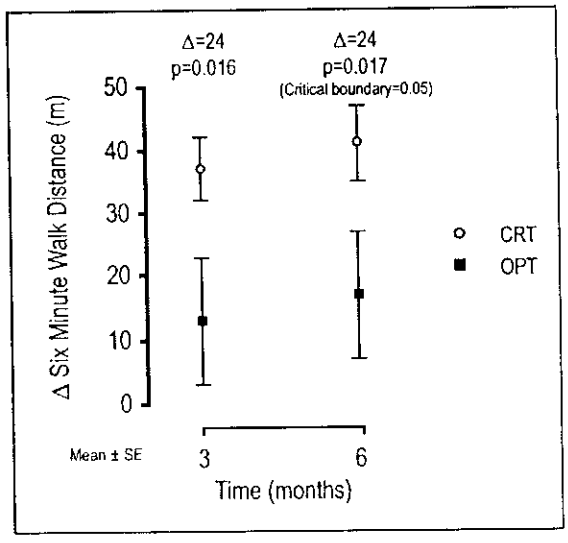

Figure 1-14. Change in Six-Minute Walk.

Table 1-12. Change in Six-Minute Walk

Six-Minute Walk (m)	CRT		OPT		
	N	Mean ± S.E.	N	Mean ± S.E.	P-value[a]
Δ at 3 months	274	37 ± 5	63	13 ± 10	0.016
Δ at 6 months	260	41 ± 5	57	17 ± 10	0.017

a. P-values obtained using one-tailed longitudinal analysis methods.

NYHA Class

The determination for New York Heart Association (NYHA) Class is based on mutual assessment, by the patient and physician, of the patient's heart failure symptoms both at rest and while performing ordinary physical activity.

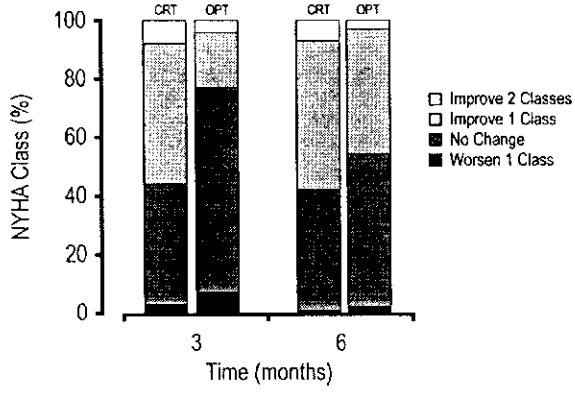

Figure 1-15. Change in NYHA.

Table 1-13. Change in NYHA

NYHA Classification	Change	CRT		OPT		P-value[a]
		N	Patients	N	Patients	
3 months	Improve 2 Classes	294	22 (7.5%)	69	3 (4.4%)	< 0.01
	Improve 1 Class		142 (48.3%)		13 (18.8%)	
	No Change		122 (41.5%)		48 (69.6%)	
	Worsen 1 Class		8 (2.7%)		5 (7.3%)	
6 months	Improve 2 Classes	291	20 (6.9%)	65	2 (3.1%)	0.032
	Improve 1 Class		149 (51.2%)		28 (43.1%)	
	No Change		118 (40.6%)		34 (52.3%)	
	Worsen 1 Class		4 (1.4%)		1 (1.5%)	

a. P-values are not adjusted for multiplicity and were obtained using a one-tailed Mantel-Haenszel chi-square method.

Quality of Life

Quality of Life (QOL) was assessed using the 21-question Minnesota Living with Heart Failure questionnaire. Each question, answered by the patient, is ranked on a scale ranging from 0 to 5. A lower total score indicates an improved quality of life.

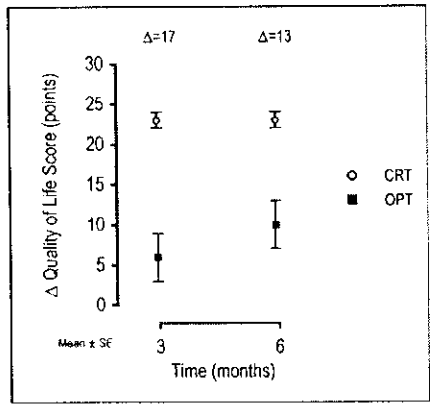

Figure 1-16. Quality of Life Score.

Table 1-14. Quality of Life Score

Quality of Life (points)	CRT		OPT		P-value[a]
	N	Mean ± S.E. (95% CI)	N	Mean ± S.E. (95% CI)	
Δ at 3 months	289	23 ± 1 (20.1, 25.7)	72	6 ± 3 (0.6, 11.3)	< 0.001
Δ at 6 months	279	23 ± 1 (19.7, 25.4)	66	10 ± 3 (4.2, 15.2)	< 0.001

a. P-values are not adjusted for multiplicity and were obtained using one-tailed longitudinal analysis methods.

Additional Functional Capacity Data

In addition to the Exercise Performance sub-study, functional capacity was evaluated by means of NYHA Class, six-minute walk distance, and Minnesota Living with Heart Failure Questionnaire© QOL for the all patients randomized to OPT and CRT-D through 6-months of follow up.

As shown in Table 1-15, NYHA Class, six-minute walk distance, and QOL scores were significantly improved in the CRT-D group compared to the OPT group at 3 and

6 months. These findings are similar to those presented in the exercise performance sub-study and previous cardiac resynchronization therapy trials.

Table 1-15. Changes in Six-Minute Walk, QOL and NYHA

Six Minute Walk Distance	CRT-D		OPT		P-value[a]
	N	Mean ± SD	N	Mean ± SD	
Δ at 3 months	420	42 ± 98	172	8 ± 82	< 0.0001
Δ at 6 months	377	45 ± 98	141	2 ± 92	< 0.0001
QOL	**N**	**Mean ± SD**	**N**	**Mean ± SD**	
Δ at 3 months	514	-24 ± 28	243	-8 ± 21	< 0.0001
Δ at 6 months	479	-23 ± 28	207	-12 ± 23	< 0.0001
NYHA	**N**	**% Improved**	**N**	**% Improved**	
Δ at 3 months	543	55	242	24	< 0.0001
Δ at 6 months	498	57	199	38	< 0.0001

a. P-values are not adjusted for multiplicity and were obtained using t-tests for continuous data and chi-square for categorical data.

CONTAK CD Study

The VENTAK® CHF/CONTAK CD®/EASYTRAK® Biventricular Pacing Study (hereafter referred to as the CONTAK CD Study) was a prospective, randomized, controlled, multicenter, double-blind study conducted at 47 sites in the United States and enrolled a total of 581 patients. Of these, 57 patients initially underwent a thoracotomy procedure to receive the Guidant Model 1822 VENTAK CHF AICD; 7 patients underwent a repeat procedure to receive an EASYTRAK lead. An additional 510 patients initially underwent an implant procedure to receive the Model 1823 CONTAK CD CRT-D along with the EASYTRAK (Models 4510/4511/4512/4513) coronary venous, single-electrode pace/sense lead for a total of 517 patients who underwent an EASYTRAK lead implant procedure. In 69 patients the EASYTRAK lead implant attempt was unsuccessful.

Table 1-16 provides information on all adverse events reported from implant through the randomization period in patients attempted or implanted with the EASYTRAK lead. During this period, a total of 765 events were reported in 310 patients. Of these, 155 were classified as complications, and 610 were classified as observations.